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THYROID STIMULATORY HORMONE (TSH) REFERENCE RANGES IN THE NORMAL PREGNANT WOMEN OF LUCKNOW

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ABSTRACT

Maternal hypothyroidism is known to be associated with adverse perinatal outcomes. This study was done to evaluate the normal reference range of TSH in pregnant women. 483 pregnant women on their first visit to Obstetrics OPD in Era's Lucknow Medical College and hospital were tested for TSH and TPO antibody using ELISA method. 25 out of 483 were positive for TPO Antibody. Of the remaining 458 patients, 142 were in first trimester, 222 were in second trimester and 94 were in third trimester. The TSH values ranged from 0.043 mIU/L to 10.1 mIU/L (mean = 2.34 mIU/L). The reference range of TSH values in all the trimesters are, 0.35 to 5.82(1st trimester), 0.28 to 5.82(2nd trimester) and 0.11 to 6.8(3rd trimester). The reference range of TSH values among the normal pregnant women of Lucknow and its surrounding areas were found to be higher than those recommended by the test kit.

KEYWORDS: TSH, TPO, Hypothyroidism

INTRODUCTION

Thyroid diseases are the second most common endocrinopathy, first being Diabetes Mellitus, to occur in women of reproductive age. Pregnancy is like a stress test for the body during which it undergoes a series of profound physiological changes. These changes have a significant effect on maternal thyroid function. If the thyroid gland is unable to adapt to these changes during pregnancy, hypothyroidism may occur (1).

Overt hypothyroidism has a prevalence of around 0.2–0.5% in pregnancy. This is other than to Subclinical hypothyroidism (SCH) which occurs in approximately 2–2.5% of pregnant women, although variations have been found in different parts of the world, such as, in China the prevalence has been reported as 4.0%, in Belgium 6.8% and in Northern Spain as high as 13.7% (2). The Prevalence is also varied in India from 16.3% in Bangalore (3) to 21.5% in Haryana (4).

It is well documented that maternal thyroid dysfunction is associated with adverse perinatal outcomes in the mother and the fetus, including miscarriage, preterm delivery, eclampsia, pre-eclampsia, and placental abruption. (5-10) Hypothyroidism in either the mother or fetus frequently results in high incidence of mental retardation. The importance of maternal thyroid hormones for fetal central nervous system development is well established (6). Rat experiments have showed that thyroid hormone receptor isoforms are present in the fetal neural tissues. The maternal T4 is converted to T3 and exerts the biological effects thus proving its role in neurodevelopmental (11). Several studies have reported decreased IQ in infants born to mothers with either overt hypothyroidism (OH) (12), hypothyroxinemia (13), or thyroid peroxidase antibody (TPO Ab) positivity (14).

Worldwide, the iodine deficiency is the most common cause of hypothyroidism in pregnant women is iodine deficiency. In the areas, iodine sufficient that are iodine sufficient the most common causes are autoimmune thyroiditis and iatrogenic causes i.e after treatment for hyperthyroidism (13).

TPO antibodies are also known as Antithyroid Peroxidase Antibodies. TPO (Thyroperoxidase) is a key enzyme in the formation of thyroid hormone and TPO is an enzyme which is responsible for the oxidation of iodide and the binding of iodine to tyrosyl residue of thyroglobulin (organification) then iodotyrosine residues undergo coupling process. TPO antibodies are present in 10-20% of women of child bearing age most of which are euthyroid (15). 16% of Euthyroid women with TPO antibody positivity develop TSH of more than 4mIU/L in the first trimester of pregnancy (16). Hence measuring TPO antibodies in euthyroid subjects can be used to identify subjects with increased risk of hypothyroidism.

As per the old guidelines, the reference ranges for TSH in the different trimesters were, first trimester – 0.1 to 2.5 mIU/L; second trimester – 0.2 to 3.0 mIU/L and third trimester – 0.3 to 3.0 mIU/L (17). But according to new guidelines, each lab should determine their own reference range as variations were found in the reference ranges depending on different geographical locations (18).

MATERIALS AND METHODS

This study was made on 483 pregnant women intheir first visit in Obstetrics and Gynecology OPD in Era's Lucknow Medical College and hospital, Hospital, Lucknow. The study was conducted with in a period of eighteen months.

Pregnant women on their first visit to Obstetrics OPD having no past history of hypothyroidism were involved in the study. Subjects such as, pregnant women on Thyroid drugs, those with past history of irradiation in the neck area and autoimmune diseases, Diabetes Melitus, Endocrine disorders, Tuberculosis or any other major illness, were excluded. Women with serum TPO antibody positivity were also excluded.

Detailed history and informed consent was taken from the patients. Fasting morning blood samples were taken from the patient. 2 ml of blood was collected in plain vacationers. The serum was separated and was immediately tested for serum TSH and TPO antibody.

TSH (Thyroid Stimulating Hormone) assay was performed by Chemiluminescence method on Beckmann Coulter Access 2. The sensitivity of the test id 0.01mIU/L.

Statistical analysis was done using SPSS 16 software. Descriptive and appropriate tests such as student t-test, chi square test etc. were applied to the data gathered and results were generated.

RESULTS

1. TSH Values In Pregnancy

In this study, we have tested 483 pregnant women, on their first visit in the Obstetrics and Gynecology OPD for serum TSH value. Out of the 483 women, 25 women were positive for TPO Antibody and were excluded from the study. The TSH values in the pregnant women ranged from a minimum 0.048 mIU/L to a maximum 10.1 mIU/L. The mean TSH value was 2.34 mIU/L with a standard deviation of 1.61 mIU/L.

2. Thyroid and Trimester

Out of the 458 pregnant women taken in our study, 142 women presented in first trimester, 222 women presented in second trimester and 94 women presented in third trimester. Change in Value of TSH in each trimester is :

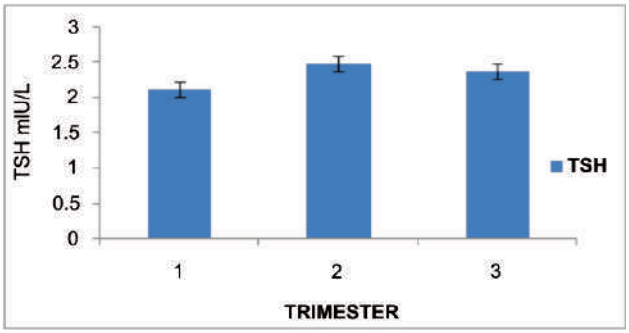

Fig 1: Comparison of TSH in Trimester

P>0.01

TSH Value in each trimester

DISCUSSION

Thyroid disorders are the second most common endocrinopathies to occur in the women of reproductive age group. Pregnancy, being a stress condition for body, increases the need of thyroid hormone. Failure to adapt to these changes leads to thyroid hormone insufficiency. Thyroid hormones, during pregnancy, are required for first 6 weeks as the fetus itself cannot produce thyroid hormones till. Till then it is completely dependent on maternal thyroid hormone for neurodevelopment (5). Thus hypothyroidism during pregnancy has a profound effect the development of fetus causing adverse pregnancy outcomes, leading to higher incidences of spontaneous abortion, preterm births, pre eclampsia, placental abruption and congenital defects.

Subclinical hypothyroidism is more prevalent that overt hypothyroidism in pregnant women (2). The most common cause of hypothyroidism worldwide is iodine deficiency. But in iodine sufficient areas, the most common causes are iatrogenic and autoimmune thyroiditis (13). The iodine and thyroid hormone demand in pregnant women increases by 50% in pregnancy (17). Thus if a woman is euthyroid initially in pregnancy, she may later develop hypothyroidism because of increased demand and decreased iodine intake. TPO antibodies are the major autoantibody present in autoimmune thyroid disorders. 10 – 20% of women of child bearing age are positive for TPO antibodies in spite being euthyroid (15). 16% of these TPO positive euthyroid women have raised serum TSH levels (>4 mIU/L) during pregnancy (16).

The objective of this study was to determine the reference range of TSH values in the pregnant women of Lucknow and its surrounding areas. amongst our 483 pregnant women. The mean TSH value found in our study was 2.46 mIU/L.

Out of the 483 women 142 women presented in 1st trimester, 222 women presented in 2nd trimester and 94 women presented in 3rd trimester.

The means of TSH values in individual trimesters were 2.12 mIU/L, 2.48 mIU/L and 2.39 mIU/L in 1st, 2nd and 3rd trimesters. There was no significant difference in the means showing that not much fluctuation is seen in the TSH values in different trimesters (p value> 0.05). The median TSH values in 1st, 2nd and 3rd trimesters are 1.82 mIU/L, 2.56 mIU/L and 1.95 mIU/L respectively. My study was in agreement with Marwaha et al., who also showed higher median TSH values in all three trimesters (19).

According to the previous American Thyroid Association guidelines, which were followed initially for diagnosis of hypothyroidism, i.e. first trimester – 0.1 to 2.5 mIU/L; second trimester – 0.2 to 3.0 mIU/L and third trimester – 0.3 to 3.0 mIU/L, the prevalence of hypothyroidism was 34.6%. [17] Using our established reference range [18], the prevalence of hypothyroidism was calculated to be 2.8%.

Studies have been done to show that reference ranges for TSH differ from laboratory to laboratory and area to area. A Study conducted in China showed reference intervals for TSH in the first, second and third trimesters were, respectively, 0·03-4·51, 0·05-4·50 and 0·47 - 4·54 mIU/l (20). Marwaha et al established reference range TSH in India, (0.6-5.0, 0.44-5.78 and 0.74-5.7 mIU/L) (19).

Lucknow and its surrounding areas are iodine sufficient areas. As the prevalence of the hypothyroidism is high in women of Lucknow, so the reference ranges should be set in each lab to help the clinicians to screening of hypothyroidism in pregnancy. Dosiou et al investigated the cost-effectiveness of targeted or universal thyroid testing in the scenario of untreated maternal hypothyroidism resulting in decreased child intelligence, with levothyroxine therapy being preventive. The study showed that Universal thyroid testing remained cost-effective in various clinical scenarios, including when only overt hypothyroidism (estimated prevalence 0.43%) was assumed to have adverse obstetrical outcomes (21).

Further the patient must be started on treatment and be monitored strictly for any signs of complications. This is supported by the fact that, randomized control trials have shown reduction in miscarriage rates on treatment with Levothyroxine in pregnant women with normal thyroid function but raised titers of TPO Abs. Two randomized studies, including a total of 187 women, evaluated the effect of levothyroxine treatment on pregnancy outcomes (22-23). Both studies showed a reduction in miscarriage rates (36% and 75% relative reductions), and when the results were pooled, there was a significant 52% relative risk reduction in miscarriages with levothyroxine (0.48, 0.25 to 0.92; P=0.03). One of the two studies reported on preterm birth (23); this study (n=115) found a 69% relative risk reduction in preterm births with levothyroxine (0.31, 0.11 to 0.90).

CONCLUSION

Our results highlight the establishment and use of appropriate trimester-specific reference ranges for TSH.

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